ANTIEPILEPTIC DRUGS

PHENYTOIN AND FOLIC ACID

The pharmacokinetics of phenytoin (PHT) before and after administration of 1 and 5 mg of folic acid is reported from the Colleges of Pharmacy and Medicine, University of Iowa, Iowa City and University of Health Sciences/The Chicago Medical School, Chicago, IL. The measured total serum PHT concentration was always greater than the calculated concentration and the days to the steady state concentration were always longer than the number calculated before folic acid was given. All subjects showed decreased serum folic acid following PHT. Since folate is assumed to be a co-factor in PHT metabolism, these results were expected because depletion of the vitamin would result in reduced metabolism of PHT and higher total serum PHT and longer time to reach steady state. When folic acid was added the same results were obtained. The depletion of folic acid had to be corrected first before its role as a co-factor in PHT metabolism could be used. (Berg MJ et al. Phenytoin pharmacokinetics: before and after folic acid administration. Epilepsia July/Aug 1992; 33:712-20.) (Reprints: Dr. M.J. Berg, College of Pharmacy, University of Iowa, Iowa City, IA 52242.)

COMMENT. The authors suggest that folic acid should be prescribed when phenytoin therapy is initiated.

CARBAMAZEPINE ACUTE TOXICITY

The clinical toxic effects and serum concentrations after ingestion of carbamazepine are reported in 82 pediatric patients from the Intensive Care Unit, Royal Children's Hospital, Melbourne, Australia. Two died, 1 of cardiac failure and 1 of aspiration pneumonitis with septicemia. In 10 patients in deep coma with a Glasgow Coma Scale (GCS) of 3-4, the mean serum level was 213 *u*mol/L. The serum carbamazepine level was related to the depth of coma, convulsions, hypotension caused by myocardial failure and conduction defects, and to the requirement for mechanical ventilation. In 27 patients with moderate coma (GCS 5-8) the mean serum level of carbamazepine was 112 *u*mol/L; convulsions occurred in 2 patients in this group. In 45 patients with mildly depressed consciousness (GCS 9-15) the serum level was 73 *u*mol/L and symptoms included drowsiness (80%), ataxia (53%), nystagmus (38%), vomiting (17%), and dystonia (7%). Patients with carbamazepine serum levels greater than 150 *u*mol/L may require intensive life support. (Tibballs J. Acute toxic reaction to carbamazepine: clinical effects and serum concentrations. J Pediatr Aug 1992; 121:295-299.) (Reprints: James Tibballs, MBBS, Intensive Care Unit, Royal Children's Hospital, Flemington Road., Parkville, Victoria, Australia 3052.)

COMMENT. In a study from the University of Cincinnati, Ohio, the administration of activated charcoal resulted in a statistically significant reduction in carbamazepine half-life but the time to complete recovery from overdose was not affected. (Wason S et al. Carbamazepine overdose - the effects of multiple dose activated charcoal. Clin Toxicol March 1992; 30:39-48.) The authors recommend no more than 2 to 3 doses (1 gram per kilogram) of activated charcoal in order to prevent